TOLERABLE UPPER INTAKE LEVEL (UL)

The highest level of nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population. As intake increases above the UL, the risk of adverse effects increases.
“AGENTS” THAT ARE POTENTIAL SOURCES OF FOOD-RELATED RISKS

[1] Natural Constituents
  ▪ Nutrients
  ▪ Non-nutrients

[2] Substances Intentionally and Directly Added

[3] Substances Indirectly Added
  ▪ Pesticides
  ▪ Indirect Food Additives

[4] Contaminants
  ▪ Naturally Occurring Chemicals
  ▪ Industrial Products, By-products
  ▪ Biological Agents
RISK ASSESSMENT INVOLVES SYSTEMATIC ORGANIZATION AND EVALUATION OF DATA

**The Agent**

- Hazards
  - What adverse effects?
- Dose-Response
  - How do severity, incidence of adverse effects change with dose?

**Population(s) Exposed to the Agent**

- Exposure
  - What dose, duration?
  - How is dose distributed?

**Risk Characterization**

- What is likelihood that exposed populations will experience adverse effects?
- How certain?
HAZARDS OF CHEMICAL AGENTS

- Many Forms of Toxicity
- Vary With the Chemical, Its Dose, and the Duration of Exposure
- Toxicity Expressed When Threshold Dose Is Exceeded
- Thresholds Vary Among Individuals
- Carcinogens May Not Exhibit Thresholds
DEVELOPMENT OF TOLERABLE UPPER INTAKE LEVELS (ULs)

Components of Hazard Identification

- Evidence of adverse effects in humans
- Causality
- Relevance of experimental data
- Pharmacokinetic and metabolic data
- Mechanisms of toxic action
- Quality and completeness of the database
- Identification of distinct and highly sensitive subpopulations
DEVELOPMENT OF TOLERABLE UPPER INTAKE LEVELS (ULs)

Components of Dose-Response Assessment

- Data selection and identification of critical endpoints
- Identification of no-observed-adverse-effect level (NOAEL) (or lowest-observed-adverse-effect level [LOAEL])
- Assessment of uncertainty and data on variability in response
- Derivation of a UL
- Characterization of the estimate and special considerations
UNCERTAINTIES

- Limitations in available HUMAN STUDIES
- Limitations in and relevance of EXPERIMENTAL DATA
- Estimating Threshold (UL) for Large, Diverse Human Population
  - VARIABILITY IN RESPONSE
  - ANIMAL-HUMAN DIFFERENCES

UNCERTAINTY FACTORS ARE USED TO DEAL WITH THESE & OTHER UNCERTAINTIES
## TOLERABLE UPPER INTAKE LEVELS (ULs) BY LIFE STAGE GROUP

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Vitamin C (mg/d)</th>
<th>&quot;-Tocopherol (Mg/d)</th>
<th>Selenium (µg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 through 6 mo</td>
<td>ND</td>
<td>ND</td>
<td>45</td>
</tr>
<tr>
<td>7 through 12 mo</td>
<td>ND</td>
<td>ND</td>
<td>60</td>
</tr>
<tr>
<td>1 through 3 y</td>
<td>400</td>
<td>200</td>
<td>90</td>
</tr>
<tr>
<td>4 through 8 y</td>
<td>650</td>
<td>300</td>
<td>150</td>
</tr>
<tr>
<td>9 through 13 y</td>
<td>1,200</td>
<td>600</td>
<td>280</td>
</tr>
<tr>
<td>14 through 18 y</td>
<td>1,800</td>
<td>800</td>
<td>400</td>
</tr>
<tr>
<td>19 through 70 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
</tr>
<tr>
<td>&gt;70 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
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</tbody>
</table>

### Pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Vitamin C (mg/d)</th>
<th>&quot;-Tocopherol (Mg/d)</th>
<th>Selenium (µg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#18 y</td>
<td>1,800</td>
<td>800</td>
<td>400</td>
</tr>
<tr>
<td>19 through 50 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
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</tbody>
</table>

### Lactation

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<tr>
<td>19 through 50 y</td>
<td>2,000</td>
<td>1,000</td>
<td>400</td>
</tr>
</tbody>
</table>
Distribution of Usual Intake

Population Potentially at Risk

Mean

UL

Intake
Dose-Response Relationship
For Adverse Effects

Population Usual Intake Distribution

UL  NOAEL  LOAEL

Intake